

REMARKS

1. Claims 43-45 have been amended to convert them into starter culture composition claims dependent on claim 25, and hence should be reinstated/rejoined.

2. In the instant case, claims 25-34 are rejected as obvious over Wessel (USP 5,580,787) in view of Donnelly (WO97/16528), further in view of Swindell (1996).

Claim 25 of the instant case is directed to

A starter culture composition comprising a lactic acid bacterium and a lactic acid bacterial helper organism that is defective in its pyruvate metabolism, said helper organism being capable of enhancing the growth rate and/or controlling the metabolic activity of the lactic acid bacterium.

Referring to the cited references, Wessels is said to teach food-safe starter cultures, comprising genetically modified lactic acid bacteria, and Donnelly an organism in which the Pfl and Ldh genes have been inactivated (thus modifying pyruvate metabolism). Swindell is said to teach manipulation of genes associated with the diacetyl metabolic pathway to achieve diacetyl production under aerobic conditions in L. lactis.

The specification defines lactic acid bacteria at page 1, lines 17-27:

As used herein the term "lactic acid bacteria" refers to gram-positive, microaerophilic or anaerobic bacteria which ferment sugars with the production of acids including lactic acid as the predominantly produced acid, acetic acid, formic acid and propionic acid. The industrially most useful lactic acid bacteria are found among *Lactococcus* species, such as *Lactococcus lactis*, *Lactobacillus* species, *Streptococcus* species, *Leuconostoc* species, *Pediococcus* species and *Propionibacterium* species. Also the strict anaerobes belonging to the genus *Bifidobacterium* is generally included in the group of lactic acid bacteria.

Donnelly's organism is Escherichia coli, which is not a lactic acid bacterium as defined above. E. coli is gram-

negative, not gram-positive as required by the definition. Moreover, its pyruvate metabolism differs from that of the LABs, as explained in the 1.132 Declaration of Claus Maxel Henriksen filed on September 19, 2001 in 08/981,098, now USP 6,645,754.

Claims 43-45 have been amended to bring them within the presently elected group. These further limit the nature of the contemplated lactic acid bacteria to particular genera (43) or species (44-45) further limits are imposed by claims 28-29. All of these claims plainly exclude Donnelly's E. coli.

The Wessels patent is directed to improved lactic acid bacteria useful as food starter cultures. The goal was to ensure the safety of recombinant strains by use of (1) an origin of replication functional in LABs but not E. coli or B. subtilis and (2) a nisin resistance gene with the same species-specific functionality. Given that the Wessels strains use origins of replication not functional in E. coli, it seems incongruous to combine the Wessels teaching with that of Donnelly.

Swindell deleted the aldB ( $\alpha$ -acetolactate decarboxylase) gene and overexpressed cloned ilrBN ( $\alpha$ -acetolactate synthase) genes in L. lactis. Swindell also discussed the diacetyl production pathway in general terms, and its Fig. 1 refers to enzymes recited in claim 27. The Examiner asserts that Swindell teaches that increased diacetyl production by L. lactis is due to the "increased activities of... NADH oxidase". We are not aware of any teachings in Swindell concerning NADH oxidase, which is not, as far as Counsel is aware, any of the enzymes of Swindell Fig. 1. Counsel believes that NADH oxidase is EC 1.6.99.3 (Ex. A, B) and Swindell's inactivated enzyme is EC 4.1.1.5 (Exs. C, D). We are not aware of any reference in Swindell to the NADH oxidase (claim 32). Nothing in Swindell discloses or suggests use of his genetically engineered L. Lactis as a helper organism in the cultivation of a second LAB. Nor does Swindell motivate use of NADH oxidase (claim 32).

The present claims are directed to a starter culture composition comprising both (1) a lactic acid bacterium, and (2)

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a LAB helper organism defective in pyruvate metabolism. The LAB helper organism (2) is capable of enhancing the growth rate and/or controlling the metabolic activity of the principal LAB (1).

The art relied-on does not clearly provide motivation to select, as a helper organism, one which is pyruvate metabolism-defective. Donnelly teaches use of his E. coli, not to stimulate growth of an LAB, but rather for industrial production of succinic acid, malic acid, or fumaric acid. And while Wessels has an LAB, and it is contemplated for use in fermented food production, he does not refer to use of mixed cultures. Swindell likewise doesn't use a mixed culture.

We respectfully remind the PTO that it granted applicants claims to the corresponding method, see Kringelum, USP 6,660,515. Claim 1 of that case read as follows:

A method of enhancing the growth rate and/or controlling the metabolic activity of a lactic acid bacterial strain, comprising cultivating the strain in association with a lactic acid bacterial helper organism that is defective in its pyruvate metabolism.

Respectfully submitted,

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Enclosure

-Declaration (with CV)

-Exs. A-D)

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